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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/509,627	04/29/2005	Peggy Wingard	006050.00067	2806

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EXAMINER	
SUTTON, DARRYL C	
ART UNIT	PAPER NUMBER
1612	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/509,627	WINGARD ET AL.	
	Examiner	Art Unit	
	DARRYL C. SUTTON	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *12-19 and 36-39* is/are pending in the application.

4a) Of the above claim(s) *14-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *12,13 and 36-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to the RCE filed 03/16/2009. New claims 37-39 have been added. Claims 1-11 and 20-35 are canceled.

Applicant's arguments filed 03/16/2009 have been fully considered. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Response to Declaration

Applicant's declaration filed 03/16/2009 has been fully considered and is not found to be persuasive.

Applicant argues that dosages of prodrug of formula I effective for producing a conscious sedated state could not have been determined from Lowrie et al. since the release kinetics differ and therefore methods of administering fospropofol disodium and propofol for achieving a conscious state could not have been predicted from data based on propofol.

The Examiner disagrees.

One of ordinary skill in the art would not be required to predict whether a conscious state could have been produced by administering fospropofol disodium by the methods of Lowrie. Only a reasonable expectation of success would be required. Since Lowrie teaches the amounts of propofol used in bolus administration, it would have been within the purview of the skilled artisan to determine the kinetic rates of propofol and fospropofol and to then determine the amount of fospropofol that would correspond to the propofol which is released into the blood of children. Bolus administration of those amounts taking into account modifications that would be required for treating any patient population that is older than a child would reasonably be expected to produce anesthesia, i.e. sedation ranging from a conscious sedated state to a deeply sedated state. Further, Stella et al. teach that substantially the same prodrug of propofol in substantially the same amounts is administered parenterally. It would have been reasonably expected that these amounts of prodrug could be delivered in a bolus parenteral injection; especially with the knowledge of the disclosure of Lowrie that propofol is delivered in a bolus injection for producing sedation.

Applicant argues that Figure 5 reveals that bolus injection of propofol produces higher maximum concentrations in plasma at a shorter time than fospropofol. This is not an unexpected result. One of ordinary skill would reasonably expect fospropofol disodium to undergo cleavage before propofol could be released into the plasma; and that some fospropofol disodium would undergo other physiological modifications in the human body, lowering the amount of propofol available. Therefore, the maximum

plasma concentration would be expected to be lower and occur at a longer time than propofol.

Applicant argues that Figure 7 reveals that patients receiving propofol injection experienced deeper sedation than those receiving fospropofol disodium. That recovery from sedation form propofol derived from fospropofol was much more gradual than that from propofol. This does not appear to be unexpected either. Since the plasma concentration of propofol is lower for fospropofol disodium it would be reasonably be expected that sedation would not be as deep as from propofol. Further, fospropofol disodium takes longer to produce a maximum plasma concentration, therefore, it would be reasonably be expected to wear off at a longer time than propofol since propofol begins to wear off even before the maximum concentration due to fospropofol disodium is achieved.

Applicants argue that figure 11 reveals that fospropofol disodium produces a slower time to maximum effect and a more gradual recovery from sedation. As discussed above, neither of these characteristics appear to be unexpected.

It would be well within the purview of one of ordinary skill in the art to determine all of the data presented above and make modifications to the amounts of the prodrug based on the data from the drug. Further, one of ordinary skill would reasonable expect that the two compounds would produce the data provided since fospropofol disodium is a prodrug that undergoes transformation in the body before propofol is released into the blood. Even without the reasonable expectation, one of skill in the art would still be motivated to administer the prodrug in amounts that overlap the claimed ranges since

Stella et al. teach amounts ranging from about 0.5 to 10 mg/kg; and would be motivated to administer the prodrug in a bolus dosage since Lowrie teaches that the method is used to produce sedation in children.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 12, 13 and 36 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Stella (US 6,204,257) in view of Lowrie (Pediatrics, 1998) and are now applicable to new claims 37-39.

Applicant argues that the propofol product label teaches away from the prior art.

The Examiner disagrees.

The label is directed to bolus administration of propofol, not of the compound of the instant claims.

Applicant argues that the demonstration of the effect of about 5 mg/kg and 10 mg/kg is commensurate in scope with the claims reciting from about 2 mg/kg to less than 15 mg/kg; and that administration of an alkali salt is commensurate in scope with a compound in its alkali salt or acid form. Targeted controlled infusion, TCI, mimics a fast bolus injection.

The Examiner disagrees.

Applicant has demonstrated that specific amounts, i.e. 5 mg/kg and 10mg/kg, are effective not all amounts of about 2 mg/kg to less than 15 mg/kg. Administering a compound as an alkali salt is not the same as administering a compound in its acid form. The argument presented in the previous office action concerning the unexpected results is still applicable (page 2 – page 3, 1st paragraph). The Examiner acknowledges Applicant's disclosure concerning TCI, however, a comparative design in which both drugs were administered in exactly the same way would have been better evidence of the advantages of one compound over the other.

Applicant argues that Lowrie fails to describe administering a bolus injection in an amount from about 2 mg/kg to less than 15 mg/kg and persons of skill would be lead away from administering higher doses.

As discussed above, Stella et al. teaches substantially the same drug in amounts that overlap the claimed ranges, i.e. from 0.5 to 10 mg/kg, administered parenterally. One of ordinary skill would be lead away from administering the compound, i.e. propofol, of Lowrie in higher bolus doses. However, he would not be lead away from a parental injection of the compound, i.e. fospropofol disodium, of Stella et al. in amounts from about 0.5 to 10mg/kg, since that is precisely what Stella et al. teaches. Further, Stella et al. does not teach that the parenteral injection is administered over any period of time, so a bolus parenteral injection would have been within the purview of one skilled in the art to produce sedation, i.e. anesthesia ranging from conscious sedation to a deep sedated state.

Applicant argues that the declaration show further evidence of the non-obviousness of the method.

Examiner has responded to the declaration above.

No claims are allowed.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Darryl C. Sutton whose telephone number is (571)270-3286. The examiner can normally be reached on M-Th from 7:30AM to 5:00PM EST or on Fr from 7:30AM to 4:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached at (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Darryl C Sutton/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612